REMARKS

Claims 6-8 are all the claims pending in the application.

Claims 6-8 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly not complying with the written description requirement. Specifically, the Examiner contends that compounds having mG1uR1 antagonism are not adequately described in the specification. The Examiner further contends that the specification does not describe any *per se* relationship between the structure and function of the mG1uR1 antagonists that may be used in the claimed methods.

Initially, and with respect to claim 7, Applicants assert that claim 7 is adequately described in the specification. Claim 7 recites the compound 6-amino-N-cyclohexyl-N, 3-dimethylthiazolo [3, 2-a] benzoimidazole-2-carboxyamide dihydrochloride which is adequately described in the specification at, for example, page 7. Therefore, Applicants assert that the subject matter of claim 7 is adequately described in the specification, and Applicants respectfully request withdrawal of this rejection.

With regard to claims 6 and 8, Applicants traverse the Examiner's rejection on the following grounds.

In light of Applicants' specification, one skilled in the art would understand those compounds which Applicants describe as useful for treating a mammal afflicted with acute stage ischemic stroke, because the present application discloses the use of mGluR1 antagonist activity for the treatment of acute stage ischemic stroke, and the term "mGluR1 antagonist" is a term of

art that embraces numerous compounds that are described in the specification and/or known in the art.

First, Applicants submit that the term "mGluR1 antagonist" is a term of art that embraces a genus of known compounds that vary significantly in structure. Applicants provide the following evidence.

Moroni *et al.*, *Neuropharmacology* 42, 741-751 (2002) (published after the present Application's filing date), reported that mGluRl antagonist compounds, which were known in the prior art and whose structures are significantly different from those structures described in the present Application (i.e. 3-MATIDA or LY-367385), reduced the volume of brain infarcts after administration 1 hour following cerebral infarction. Thus, this document illustrates that the art recognizes the term "mGluR1 antagonist" and that the term embraces several known compounds. Also See Moroni *et al.*page 742, left column, second full paragraph.

Moroni *et al.*, *J. Pharmacol. Exp. Ther.* 281(2), 721-729 (1997) uses the term "mGluRl antagonist" in the title and shows, at page 728, left column, last paragraph, that AIDA is the most potent and selective mGluRl antagonist. Thus, the term "mGluR1 antagonist" is a term of art, and embraces the compound AIDA.

Clark *et al., Bioorg. Med. Chem. Lett.* 7(21), 2777-2780 (1997) uses the term "antagonist...at mGluRl receptors" in abstract and in the last paragraph of page 2777, and describes the compounds (S)-4CPG and α-methy l-4-carboxyphenylglycine (LY367385) as potent mGluRl antagonists. Furthermore, page 2779, Table 1, shows compounds with increased selective antagonist activity at mGluR1α over mGluR5a, and at page 2780, concludes that

LY367385 and Compound 2 are more potent and selective mG1uR1 antagonists than other "phenylglycines." Thus, the term "mGluR1 antagonist" is a term of art that embraces particular compounds such as S-4CPG and LY367385.

Bernstein *et al.,* Neuropharmacology 37, 169-178 (1998) uses the term "mGluR1 antagonist" in the abstract (line 5), and describes that 4CPG and 4C3HPG are selective mGluR1 antagonists (see, for example, page 175, left column, lines 3-8). Thus, the term "mGluR1 antagonist" is a term of art that embraces particular compounds such as 4CPG and 4C3HPG.

Salt *et al., Neuroscience* 85(3), 655-658 (1998) shows that S-2-methyl-4-carboxy-phenylglycine is an antagonist having a high specificity to metabotropic glutamate receptor 1 (mGluR1). See Abstract, lines 14-15. Thus, S-2-methyl-4-carboxyphenylglycine is an MGluR1 antagonist known in the art.

Pellicciari *et al., Bioorg. Med. Chem. Lett* 8, 1569-1574 (1998) uses the term "selective mGluR1 antagonist" in the title and in the abstract (see lines 18-19) and shows that the compound ACUDA is a selective mGluRl antagonist. For example, Fig. 1, right panel, shows that ACUDA is a selective antagonist on mGluR1b, and Fig. 2 shows that mGluR1 antagonist (S)-CBPG has higher mGluR1 antagonist activity than ACUDA. Thus, the term "mGluR1 antagonist" is a term of art that embraces particular compounds such as ACUDA and (S)-CBPG.

Therefore, in view of the above, Applicants submit that the term "mGluR1 antagonist" is known in the art to embrace a particular genus of compounds. Accordingly, Applicants respectfully assert that the instant application complies with the written description requirement, and respectfully request withdrawal of this rejection.

Second, Applicants respectfully submit that the facts surrounding the present application are different from those of the Federal Circuit's recent decision in *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916 (Fed. Cir. 2004).

In *University of Rochester*, the Federal circuit held that the written description requirement was not satisfied with respect to claims directed to methods of selectively inhibiting PGHS-2 activity by administering selective COX-2 inhibiting compounds, because the specification did not describe any such compounds, and no such compound was known in the prior art. In denying the University of Rochester's cross-motion for summary judgment, the Federal circuit stated that "The patent's claims all require a COX-2-selective compound, but no COX-2-selective compound is disclosed in the patent, and it is undisputed that there was no pre-existing awareness in the art of any compound having COX-2-selective activity." *U. of Rochester*, 358 F.3d 916 at 927.

However, in the present case, mGluR1 antagonists were known to one of ordinary skill in the art at the time the priority application was filed (see above), and the specification describes, by way of example, specific mGluRl antagonists useful for the treatment of ischemic infarction in the pathologic model. For example, page 3, first full paragraph, describes the mGluR1 antagonists AIDA and 4CPG; page 7, *inter alia*, describes the mGluR1 antagonist 6-amino-N-cyclohexyl-N, 3-dimethylthiazolo [3, 2-a] benzoimidazole-2-carboxyamide dihydrochloride; the bottom of page 8 to the top of page 9 cites the documents WO 95/25110, WO 96/15099, WO 96/15100, WO 97/05109, WO 97/05137, WO 98/06724, and Japanese Application 9-357552, which describe mGluR1 antagonists; and page 9-10 describes an exemplary structural formula

for some mGluR1 antagonists. Therefore, whereas, in the *University of Rochester* decision, no selective COX-2 inhibitors were described in the specification nor known in the art, in the present case, numerous mGluR1 antagonists are described in the specification as well as known to one of ordinary skill in the art.

Therefore, Applicants assert that the Application satisfies the written description requirement as to claims 6 and 8, and Applicants respectfully request reconsideration and withdrawal of this rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

Mark L. Hayman
Registration No. 51,793

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: April 6, 2004